Tracking down pathogenic yeasts

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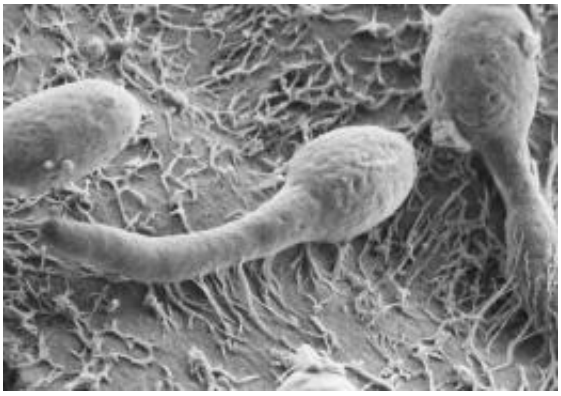

Candida albicans (© Fraunhofer IGB)

If the human immunological system is weakened, yeast fungi that are normally harmless can be transformed into a lethal danger. This is why researchers at Fraunhofer are using next-generation sequencing to track down one of the most frequent pathogens for fungal infections among humans.

More than half of all people are hosts to Candida albicans in their bodies. This species might be located on their skin or mucous membranes or in the intestines - frequently without causing any symptoms. However, it can be dangerous to patients whose immunological system has been weakened such as after organ transplants or chemotherapy with cancer. Then, this fungus penetrates into deeper layers of tissue and uses the blood system to spread throughout the body. In Germany alone, several thousand people die from systemic candida

infections every year.

But why does Candida albicans become lethal to people? Which genes are active in the pathogenic state? Are there any interactions between the host and the fungus? What protective mechanisms might prevent the pathogenic state in humans? Researchers at the Fraunhofer Institute for Interfacial Engineering and Biotechnology (IGB) in Stuttgart, Germany, asked themselves these and other questions applying pioneering sequencing technology.

This technology is a real game-changer because it can be automated and it greatly accelerates the analysis of genotypes. A case in point is decoding a person's genome and determining the sequence of bases of DNA, which can now be done within a couple weeks. As a comparison, five large-scale research centers with 150 coworkers have been working at sequencing the human genome for seven years, and the Humane Genome Project cost approximately $3 billion. The sequence of the approximately 3 million bases of the human genome was made public in 2001.

Researchers at the Fraunhofer Institute for Interfacial Engineering and Biotechnology have been taking advantage of this cutting-edge sequencing technology to find out which genes play a role in causing the disease to break out with the fungus and the host. Researchers are working with system biology scenarios that they hope will help explain the essential pathogenic mechanisms. The researchers start off by isolating the mRNA, i.e., the copies of all of the active genes, from the human pathogenic yeasts. Then they transform the mRNA into DNA to subsequently fragment and sequence them. What‘s tricky with this Next-Generation sequencing is the fact that it is not just a couple of fragments that are sequenced, but millions of DNA fragments simultaneously. A single strand of DNA acts as a matrix and an enzyme resynthesizes the second DNA strand on it, one building block after another in a very tight

space. To follow this process, each of the four different building blocks (the bases adenine A, guanine G, cytosine C or thymine T) is marked with a different fluorescent dye, and a detector captures all of the various light signals. This is how the sequence of bases can be read from each fragment. The stupendous quantities of data are then analyzed with bioinformational techniques, and researchers can directly discover which genes are still active.

Biologist Christian Grumaz of the Fraunhofer Institute for Interfacial Engineering and Biotechnology provides an explanation for this: "At top speed, we can use this Next-Generation DNA sequencer to simultaneously sequence as many as 100 million DNA fragments with a reading length of up to 500 bases." His institute colleague Dr. Kai Sohn adds, "For the first time, this method enables us to simultaneously obtain both highly sensitive transcription profiles from human pathogenic fungi and infected host cells." Researchers are hoping that this will enable them to draw key conclusions on why the fungus is so dangerous for certain persons with a weakened immunological system.

Scientists will be unveiling their findings at the joint Fraunhofer stand in Hall 9, Stand 30 while graphically demonstrating the huge amounts of data that Next-Generation sequencing supplies. Beyond this, 10 books show examples of the transcriptome of Candida. Other topics that will be discussed at their stand include clinical tests for diseases of the respiratory passages, in vitro testing systems, utilizing nature as a chemical factory, biochips for individualized breast cancer therapy, DNA microarrays for quick diagnosis of pathogens, and 3-D skin models.

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https://phys.org/news/2010-09-tracking-pathogenic-yeasts.html